

July 5, 1954

Dear Professor Hinshelwood:

I have been struck by the degree to which current controversies on the mechanism of bacterial adaptation may be at cross-purposes owing to the divergence of experimental material, a situation that might be readily corrected. If I may take the liberty of the remark, your observations on the adaptation of *B. lactis aerogenes* to the utilization of D-arabinose represent the clearest support of your arguments; the multistep variations involved in resistance to proflavine would require a much more elaborate review. At any rate, if I can find the time, I would like the opportunity of reviewing the situation on my own laboratory bench— particularly the experiment represented by figure 1 in the paper by Baskett and yourself, PRS, B139:58. May I ask your assistance in furnishing the strain you used for these experiments? To avoid any confusion, I should also like to have for comparison a subculture of what you would certify to be an irreversibly "trained" strain.

The S.E.B. issue on Evolution has just come to our library, and I was most pleased to see the clarity with which you presented the issue (though I will not pretend that your argument and conclusion are such that I can fully acquiesce in them), especially at page 32, that we are concerned at the means of irreversibility. Noone has questioned that physiological adaptations occur, nor that they are represented in your experiments, but this very fact tends to confuse the experimental decision. In most of your work, my attempted interpretation (as you know) would be that induced physiological adaptations had permitted the development of populations large enough that spontaneous variations might then occur and be selectively fixed, a mechanism hardly distinguishable from Waddington's findings on *Drosophila* (at pp.194-198 of the same symposium). I would not argue that genetic factors are required by natural law to be so insulated from the day to day history of the cell; but my reading of the evidence is that this is what happens to have come about during the evolution of living forms. I can assure you that I would be quite prepared to entertain evidence to the contrary, but so far (with some tortuosity to be sure!) the mutation theory does not seem to me to have failed. However, I could comment on this with less prejudice if I could reexamine relevant material with my own hand.

May I take the occasion to renew my request for reprints, a favor I am happy to reciprocate. I lack the following that have appeared in the Proc. Roy. Soc.: (Dean and Hinshelwood) 1952 140:339; (Hinshelwood and Jackson) 137:88; 136:562; and (Kilkenny and Hinshelwood) 139:575, in addition that others that may have appeared subsequently.

I have noted your correction in Nature as to your "disregard" of selection mechanism. If "Bacterial Physiology" could be revised, I would rewrite this chapter to fit more closely to your current views; I have had an opportunity to substitute "minimized" in later printings, which I hope does not effect too much of a distortion. I should have quoted your letter of 16 Feb 1949 in the wording "to explore the potentialities" in place of "to bolster the applicability": perhaps I was influenced by your paper with Peacocke (1948) which seemed, in a very different spirit (and to my mind wholly without justification) to deny the materiality of the auxotrophic mutants that are the daily utensils of microbial genetics! However, your subsequent writings, including the letter to Nature seem to have adopted a "more eclectic outlook", so I trust there need be no further quarrel. By the way, you do me too much honor in attributing "Bacterial Physiology" to my authorship.

I do not have the final corrected volume, but the proofs of the S.G.M. symposium of last year contained in line (your paper with Dean. the terminal

"A synthetic agar plate was spread with  $2 \times 10^7$  [sic] cells.... single colonies were spread visible on this plate". Can you distinguish so many single colonies on a plate, or is the figure a typographical error? If so few cells were inoculated that single colonies were developed, the experiment is indecisive (from the selectionist viewpoint) since any mutants transferred to the replica plate must have constituted a negligible proportion of the colony during whose growth they must have arisen. If there were  $2 \times 10^7$  colonies (which I suppose could be distinguished under the microscope), I don't see how one could maintain so precise a correspondence, after two replicas, that one could expect congruence by a factor of  $5/2 \times 10^7$ , that is a resolution of this fraction x the area of a Petri dish,  $= 75 \text{ cm}^2$ , or about  $(0.4 \text{ mm})^2$ . But even accepting this technical tour de force, the next plating suggests that these 5 colonies altogether had less than 1% mutant cells, which is quite compatible with the possibility of a mutant having arisen some time after the  $16-32$  cell stage of any of the colonies. The later history of the single colony of the 100 whose replica did show a resistant shows that this colony did not come from a mutant cell, but that a new mutation had

1. The first thing I noticed when I stepped out of the car was the cold. It was a sharp, biting cold that seemed to penetrate my coat. I shivered as I walked towards the entrance of the building. The air was thick with the scent of old books and the faint, sweet smell of incense. I had heard that the library was a place of great knowledge, but I had not realized how much it was also a place of great mystery.

2. As I entered the main hall, I was struck by the sheer scale of the place. The ceiling was high, with intricate carvings and a large, ornate chandelier hanging from the center. The walls were covered in bookshelves that reached up to the very top of the room. The shelves were filled with books of all sizes, colors, and thicknesses. It was a vast sea of knowledge, and I felt a sense of awe and wonder as I walked through the aisles.

3. I was led to a small, quiet room at the back of the building. The room was dimly lit, with a single lamp on a small table. The walls were covered in bookshelves, and the floor was made of polished wood. A large, comfortable-looking chair sat in the center of the room, and a small table with a book and a glass of water was next to it. I felt a sense of peace and tranquility as I sat down and began to read.

4. The book was a thick, old volume with a worn leather cover. The pages were yellowed with age, and the ink was a deep, rich brown. I turned the first page and was greeted by a beautiful illustration of a landscape. The scene was peaceful and idyllic, with a small village nestled in a valley. The sun was setting, and the sky was a mix of orange and red. I felt a sense of calm and serenity as I looked at the picture.

5. As I continued to read, I began to feel a sense of connection to the world depicted in the book. The characters were so real, so alive, that I felt like I was part of their story. I was drawn into their world, and I found myself caring about their fate. The author had a way of writing that made the reader feel like they were right there with the characters, experiencing everything as if it were their own.

6. The night was quiet, and the only sound was the soft rustle of the pages as I turned them. I felt a sense of peace and tranquility that I had never experienced before. The world outside the library was a blur, and I was completely absorbed in the story. I had found a place where I could escape from the worries of the world and immerse myself in a world of pure imagination.

7. As the first light of dawn began to break, I closed the book and looked up at the ceiling. The chandelier was still lit, and the room was still quiet. I felt a sense of peace and tranquility that I had never experienced before. I had found a place where I could escape from the worries of the world and immerse myself in a world of pure imagination.

8. I stood up and walked towards the door. The room was still quiet, and the only sound was the soft rustle of the pages as I turned them. I felt a sense of peace and tranquility that I had never experienced before. I had found a place where I could escape from the worries of the world and immerse myself in a world of pure imagination.

9. As I walked out of the library, I felt a sense of peace and tranquility that I had never experienced before. I had found a place where I could escape from the worries of the world and immerse myself in a world of pure imagination.

10. The world outside the library was a blur, and I was completely absorbed in the story. I had found a place where I could escape from the worries of the world and immerse myself in a world of pure imagination.

1. The first of the two main reasons for the failure of the first two attempts at a coup d'état in 1961 and 1962 was the lack of support from the army. The army was not united behind the coup and many officers were loyal to the government.

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 Yours sincerely,  
 Joshua Lederberg

Professor of Genetics

1. The first part of the report, "The Situation in the Field," describes the current state of the conflict in the region. It notes that the fighting has intensified since the beginning of the year, with significant casualties on both sides. The report also mentions the displacement of thousands of civilians and the destruction of infrastructure.